REMARKS

The instant application is a Continued Prosecution Application (CPA) under 35 CFR 1.53(d), based upon a prior application Serial No.: 09/415,540. The Examiner indicated that the filing date of the instant application was January 9, 2001. Applicants respectfully request that the Examiner cite the current Attorney Docket Number: PF-0148-3 CPA, and the filing date for the present CPA in future communications. The cooperation of the Examiner is appreciated.

Claims 1 and 18-22 are pending in the application. Claims 1 was withdrawn as being drawn to non-elected inventions. Applicants reserve the right to prosecute the non-elected claims in subsequent divisional applications. Claims 18-22 have been amended to clarify the subject of the claimed invention. No new matter is added by these amendments. Entry of these amendments is respectfully requested. Therefore, claims 18-22 are currently being examined on the merits.

Written description rejections under 35 U.S.C. § 112, first paragraph:

Claims 18-22 are rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking adequate written description. Regarding claim 19, the Examiner argues that the claimed genus was not sufficiently described "because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claims." (Office Action at page 3). Regarding claims 18, and 20-22, the Examiner asserts that "a naturally-occurring DNA encoding a polypeptide comprising a sequence having 90% identity to SEQ ID NO:1 and a method of use of a probe comprising 15, 30 or 60 nucleotides of SEQ ID NO:2 lack sufficient written description needed to practice the invention of claims 18, and 20-22." (Office Action at page 3). Applicants respectfully traverse.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met.

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

Applicants respectfully point out that claim 19 recites "an isolated polynucleotide selected from the group consisting of: a) a polynucleotide sequence of SEQ ID NO:2, b) a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 and c) a polynucleotide sequence complementary to a) or b). The Specification (page 11, line 26 to page 12, line 3) discloses that:

> It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of nucleotide sequences encoding HPYP, some bearing minimal homology to the nucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of nucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet genetic code as applied to the nucleotide sequence of naturally occurring HPYP, and all such variations are to be considered as being specifically disclosed.

While all such sequences are not explicitly listed, given the amino acid sequence of SEQ ID NO:1 and the exemplary polynucleotide sequence of SEQ ID NO:2, one of ordinary skill in the art could predict all such sequences using the known genetic code.

Furthermore, the skilled artisan could just as easily predict the complementary sequences, since this would involve a merely mechanical substitution of complementary nucleotide bases.

Thus the subject matter of claim 19 is also adequately described.

Applicants further note that claim 19 recite naturally-occurring variants. Thus the genus does not comprise every conceivable variant which might be made using recombinant methods, as all that is claimed are those variants which are found in nature. The identification of these naturally-occurring polynucleotides encoding polypeptide variants with at least 90% amino acid sequence identity to SEQ ID NO:1 would be routine for one skilled in the art based on the disclosure of the polypeptide of SEQ ID NO:1 and the polynucleotide of SEQ ID NO:2 in the instant application. While identifying a polynucleotide sequence, and the polypeptide encoded by the polynucleotide sequence, was a major undertaking at one time (even given partial nucleotide sequence data), modern methods of high-throughput nucleic acid sequencing and sequence assembly have greatly simplified the process. In fact, at the time the instant application was filed, an entire industry had already developed around the identification and testing of variant polynucleotides and polypeptides. There are countless examples of how polynucleotides and/or polypeptides of a genus have been isolated based on known properties of a species. The necessity of withholding proprietary polynucleotide and polypeptide sequence and functional data prior to obtaining some degree of patent protection is evidence of the ease and speed with which one skilled in the art can identify additional member of a genus of polynucleotide and polypeptide sequences (*e.g.*, from genomic and cDNA libraries) given the disclosure of a species identified through diligent research efforts.

The disclosure of the instant application contains, *inter alia*, the essential elements that would allow one skilled in the art to identify expressed variant polynucleotides and polypeptides from cDNA libraries: (I) polynucleotide and polypeptide sequence data to facilitate the design of oligonucleotide primers for the identification of variants (*e.g.*, polynucleotides that encode polypeptides with 90% sequence identity to SEQ ID NO:1), (ii) knowledge of the tissue-specific expression pattern of the polynucleotides and polypeptides to allow the selection of an appropriate cDNA library from which to identify these variants (*e.g.*, the expression pattern described in page 11 of the specification of the above identified application), (iii) an assay for the identification of variants of SEQ ID NO:1 with the disclosed biological properties (described on pages 44-45 of the specification), and (iv) in the case of claim 41, an additional conserved HPYP structural motif and hydrophobicity plots as defined in the Specification at page 11, lines 7-12

and in Figures 3A and 3B. Thus, given the disclosure of the instant application, it would be routine for one skilled in the art to identify variants as claimed in claim 19.

Similarly, regarding claims 18, and 20-22, the specification provides ample description for the claimed invention. Independent claim 20, and dependent claims 18, and 21-22 recite a method of detecting a target polynucleotide in a sample using a probe comprising a sequence complementary to the target polynucleotide. Such methods are described on page 21, lines 10-17:

"The presence of the polynucleotide sequence encoding HPYP can be detected by DNA-DNA or DNA-RNA hybridization or amplification using probes or portions or fragments of polynucleotides encoding HPYP. Nucleic acid amplification based assays involve the use of oligonucleotides or oligomers based on the HPYP-encoding sequence to detect transformants containing DNA or RNA encoding HPYP. As used herein "oligonucleotides" or "oligomers" refer to a nucleic acid sequence of at least about 10 nucleotides and as many as about 60 nucleotides, preferably about 15 to 30 nucleotides, and more preferably about 20-25 nucleotides, which can be used as a probe or amplimer."

Further, applicants describe how to make the probes in the methods of detection in the specification from page 33, line 26 to page 34, line 3.

"Means for producing specific hybridization probes for DNAs encoding HPYP include the cloning of nucleic acid sequences encoding HPYP or HPYP derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, commercially available, and may be used to synthesize RNA probes in vitro by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, radionuclides such as 32P or 35S, or enzymatic labels, such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like."

Lastly, applicants provide exemplary teachings on page 43, Example VI on how to label and use the hybridization probes.

Thus the disclosure of the instant application satisfies the written description requirements under 35 U.S.C. § 112, first paragraph, based on the literal disclosure in the specification and what was known in the art at the time the application was filed. For at least these reasons, Applicants request withdrawal of the rejections.

Enablement rejections under 35 U.S.C. § 112, first paragraph:

Claims 18, 20-22 are rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. The Examiner asserts that "the specification does not support the broad scope of the claim which encompass all modifications and fragments of any sequence that comprises a fragment of SEQ ID NO:2." (Office Action, page5). The Examiner argues that "the properties of a polypeptide of an unknown length and structure are unpredictable based on a fragment." (Office Action, page 6).

The Examiner is mistaken on two grounds. First, Applicants have provided ample teaching regarding the structural features and functions of the polypeptides encoded by the claimed polynucleotides, as remarked above in this response. Second, and more importantly, Applicants respectfully point out that the claims are directed to polynucleotides, and methods of detection using such polynucleotides, not polypeptides; thus the functionality of the encoded polypeptides is not the sole determinant of the claimed genus. Members of the claimed genus may include, for example, mutant alleles associated with diseases, or single nucleotide polymorphisms (SNPs). Such alleles are well known in the art. It is not necessary to describe specific examples of the members of this genus, since one of skill in the art would reasonably understand what is encompassed by the claims.

Applicants also note that claim 19 recite naturally-occurring variants. Thus the genus does not comprise every conceivable variant which might be made using recombinant methods, as all that is claimed are those variants which are found in nature. Given the sequences of SEQ ID NO:1 and SEQ ID NO:2, as well as the structural descriptions provided on page 11 of the specification, and the protocols on page 43, one of ordinary skill in the art could readily identify a naturally occurring polynucleotide encoding a polypeptide having at least 90% identity to SEQ ID NO:3, and to practice the methods of detection as claimed herein, using well known methods of sequence analysis, without any undue experimentation. Contrary to the Examiner's assertion that there are "essentially infinite possible choices" encompassed by the claimed invention, the instant invention encompass well-defined variants as supported by the specification. The skilled artisan would also know how to use the claimed polynucleotides, for example in expression profiling as discussed above.

For at least the above reasons, withdrawal of the enablement rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Withdrawn Rejections under 35 U.S.C. § 102:

Applicants thank the Examiner for withdrawing the rejections of claims 18-22 under 35 U.S.C. 102 (b) over Yang et al.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650)855-0555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

This form is enclosed in duplicate.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

18. (Reiterated) The method of claim 20, wherein before hybridization, the target polynucleotide is amplified by the polymerase chain reaction.

19. (Reiterated) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide sequence of SEQ ID NO:2,

b) a naturally-occurring human polynucleotide sequence variant encoding an amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:1 and

c) a polynucleotide sequence complementary to a) or b).

20. (Reiterated) A method of detecting a target polynucleotide in a sample, said target polynucleotide having the sequence of a polynucleotide of claim 19, comprising

hybridizing the sample with a probe comprising at least 15 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide, and

detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

21. (Reiterated) A method of claim 20, wherein the probe comprises at least 30 contiguous nucleotides.

22. (Reiterated) A method of claim 20, wherein the probe comprises at least 60 contiguous nucleotides.